CLAIMS

What we claim is:

1. A process for preparing an agglutinogen preparation from a Bordetella strain, comprising the steps of:
(a) providing a cell paste of the Bordetella strain;
(b) selectively extracting fimbrial agglutinogens from the cell paste to produce a first supernatant containing said agglutinogens and a first residual precipitate;
(c) separating the first supernatant from the first residual precipitate;
(d) incubating the first supernatant at a temperature and for a time to produce a clarified supernatant containing fimbrial agglutinogens and a second precipitate containing non-fimbrial agglutinogen contaminants;
(e) concentrating the clarified supernatant to produce a crude fimbrial agglutinogen solution; and
(f) purifying fimbrial agglutinogens from the crude fimbrial agglutinogen solution to produce the fimbrial agglutinogen preparation.

2. The process of claim 1 wherein said incubation step (d) is effected at a temperature of about 75°C to about 85°C.

3. The process of claim 2 wherein the temperature is about 80°C.

4. The process of claim 2 wherein said incubation step (d) is effected for a time of about 10 minutes to about 60 minutes.

5. The process of claim 3 wherein the time is about 30 minutes.

6. The process of claim 2 wherein the fimbrial agglutinogens are selectively extracted in step (b) by dispersing the cell paste in a buffer comprising about 1M to about 6M urea.

7. The process of claim 2 wherein the first supernatant is concentrated prior to the incubation step (d).

8. The process of claim 7 wherein the concentration step (e) is effected by precipitating fimbrial agglutinogens from the clarified supernatant, separating the precipitated fimbrial agglutinogens from the resulting supernatant, and solubilizing the precipitated fimbrial agglutinogens.

9. The process of claim 8 wherein said precipitation is effected by the addition of a polyethylene glycol to the clarified supernatant.

10. The process of claim 8 wherein said precipitation is effected by adding polyethylene glycol of molecular weight about 8000 to the clarified supernatant to a concentration of about 3% to about 5 wt% to effect precipitation of said agglutinogens from the clarified supernatant.

11. The process of claim 10 wherein the concentration of polyethylene glycol is about 4.3 to about 4.7 wt%.

12. The process of claim 1 wherein the agglutinogens are purified from the crude fimbrial agglutinogen solution by column chromatography.

13. The process of claim 12 wherein said column chromatography includes Sephadex 6B and/or PEI silica column chromatography.

14. The process of claim 12 wherein said purification step includes sterilization of run through from said column chromatography purification to provide a sterile fimbrial agglutinogen preparation.

15. The process of claim 14 wherein said sterile fimbrial agglutinogen preparation is absorbed onto a mineral salt adjuvant.

16. The process of claim 15 wherein said mineral salt adjuvant is alum.

17. The process of claim 1 wherein the Bordetella strain is a strain of Bordetella pertussis.

18. A fimbrial agglutinogen preparation from a Bordetella strain comprising fimbrial agglutinogen 2 (Agg

2) and fimbrial agglutinogen 3 (Agg 3) substantially free from agglutinogen 1.

19. The preparation of claim 18 wherein the weight ratio of fimbrial Agg 2 to fimbrial Agg 3 is from about 1.5:1 to about 2:1.

20. The fimbrial agglutinogen preparation of claim 19 produced by a method of claim 1.

21. An immunogenic composition comprising the agglutinogen preparation of claim 18, 19 or 20.

22. The immunogenic composition of claim 21 formulated as a vaccine for in vivo use for protecting a host immunized therewith from disease caused by Bordetella.

23. The immunogenic composition of claim 22 further comprising at least one other Bordetella antigen.

24. The immunogenic composition of claim 23 further comprising at least one non-Bordetella antigen.

25. The immunogenic composition of claim 23 further comprising an adjuvant.

26. The immunogenic composition of claim 25 wherein the adjuvant is selected from the group consisting of aluminum phosphate, aluminum hydroxide, Quil A, QS21, calcium phosphate, calcium hydroxide, zinc hydroxide, a glycolipid analog, an octodecyl ester of an amino acid and a lipoprotein.

27. A vaccine composition for protecting an at-risk human population against a case of disease caused by infection by B. pertussis, which comprises pertussis toxoid, filamentous haemagglutinin, pertactin and agglutinogens of B. pertussis in purified form in selected relative amounts to confer protection to the extent of at least about 70% of members of the at-risk population.

28. The vaccine of claim 27 wherein said pertussis toxoid is present in an amount of about 5 to about 30 μg nitrogen, said filamentous haemagglutinin is present in an amount of about 5 to about 30 μg nitrogen, said

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pertactin is present in an amount of about 3 to about 15 µg nitrogen and said agglutinogens are present in an amount of about 1 to about 10 µg nitrogen, in a single human dose.

29. The vaccine of claim 28 containing about 10 µg nitrogen of pertussis toxoid, about 5 µg nitrogen of filamentous haemagglutinin, about 5 µg nitrogen of pertactin and about 3 µg nitrogen of agglutinogens in a single human dose.

30. The vaccine of claim 28 containing about 20 µg nitrogen or pertussis toxoid, about 20 µg nitrogen of filamentous haemagglutinin, about 5 µg nitrogen of pertactin and about 3 µg nitrogen of agglutinogens in a single human dose.

31. The vaccine of claim 27 wherein the extent of protection is at least about 80% for a case of pertussis having a spasmodic cough of duration at least 21 days and confirmed bacterial infection.

32. The vaccine of claim 27 wherein the extent of protection is at least about 70% for a case of mild pertussis having a cough of at least one day duration.

33. The vaccine of claim 28 wherein the extent of protection is about 85% for a case having a spasmodic cough of duration at least 21 days and confirmed bacterial infection.

34. The vaccine of claim 27 wherein said agglutinogen comprise fimbrial agglutinogen 2 (Agg 2) and fimbrial agglutinogen 3 (Agg 3) substantially free from agglutinogen 1.

35. The vaccine of claim 34 wherein the weight ratio of Agg 2 to Agg 3 is from about 1.5:1 to about 2:1.

36. The vaccine of claim 27 further comprising tetanus toxoid and diphtheria toxoid.

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37. The vaccine of claim 36 wherein said diphtheria toxoid is present in an amount of about 15 Lfs and tetanus toxoid is present in an amount of about 5 Lfs.

38. The vaccine of claim 27 further comprising an adjuvant.

39. The vaccine of claim 38 wherein the adjuvant is alum.

40. A method of immunizing a host against disease caused by Bordetella, comprising administering to the host an immunoeffective amount of the immunogenic composition of claim 21.

41. The method of claim 40 wherein the host is a human.

42. A method of immunizing an at-risk human population against disease caused by infection by B. pertussis, which comprises administering to members of the at-risk human population an immunoeffective amount of the vaccine composition of claim 47 to confer protection to the extent of at least about 70% of the members of the at-risk population.